REMARKS

Following entry of the foregoing amendments, claims 1, 2, and 4 to 7 will be pending in the application. Claim 1 has been amended, and claims 3 and 8 to 20 have been canceled, herein, without prejudice, to remove non-elected subject matter. Claim 7 has been amended to place the claim into independent form. No new claims have been added.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

Alleged Indefiniteness

Claims 1 to 7 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for recitation of the term "prodrug." The Office Action asserts that the particular groups to which the term refers, and their positions on the compounds of formula I, are unclear. Without conceding the correctness of the assertion, claims 1, 5, and 6 have been amended, as suggested in the Office Action, to replace the term "prodrug" with the term "ester." Support for the amendment is found throughout the specification as originally filed, including, for example, paragraph 19. The rejection has been obviated, and Applicants respectfully request withdrawal thereof.

Alleged Anticipation

A. Claims 1, 3 to 5, and 7 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Mellor, H.R., *et al.*, *Analytical Biochemistry* 284:136-142 (2000) (hereinafter "the Mellor article"). The Office Action asserts that page 139 of the Mellor article describes 2S and 5S polyhydroxypiperidine compounds encompassed by the claims.

Applicants respectfully traverse the rejection because Table 1 on page 139 of the Mellor article depicts four polyhydroxypiperidines, none of which are defined by the claims. For example, the stereochemistry of the substituent at position 2 of the first two polyhyroxypiperidines shown in the table, N-butyl-deoxynojirimycin and N-butyl-deoxygalactonojirimycin, is opposite to that of the compounds of formula I of claim 1. In addition, the substituent at position 2 of the fourth polyhydroxypiperidine shown in Table 1 of the article, N-butyl-6-methyl-galactonojirimycin, is a methyl group, rather than the $-CH_2OH$ group of the compounds of formula I. Finally, the third polyhydroxypiperidine shown in Table 1, N-butyl-idonojirimycin (3,4,5-piperidinetriol, 1-butyl-2-(hydroxymethyl)-, (2S,3R,4R,5S)) is specifically excluded from claim 1 by proviso (a), and is not recited in claims 5 and 6. In addition, as recited in claim 7, pharmaceutical formulations containing N-butyl-idonojirimycin are not taught or suggested in the Mellor article because the article fails to ascribe any therapeutic utility whatsoever to N-butyl-idonojirimycin. Accordingly, the Mellor article fails to teach or suggest the subject matter defined by the claims, and Applicants respectfully request withdrawal of the rejection.

B. Claims 1 to 7 have been rejected under 35 U.S.C. § 102(e) as allegedly anticipated by published PCT application number WO 01/10429 (hereinafter "the Zitzmann application"). The Office Action asserts that the application describes N-nonyl-altrostatin in Figure 1. Applicants respectfully traverse the rejection because N-nonyl-altrostatin (3,4,5-piperidinetriol, 1-nonyl-2-(hydroxymethyl)- (2S,3S,4R,5S)) is specifically excluded from claims 1 and 7 by proviso (c) and is not recited in claims 5 and 6. Accordingly, the Zitzmann

application fails to teach or suggest the subject matter defined by the claims, and Applicants respectfully request withdrawal of the rejection.

Alleged Obviousness

Claims 1 to 7 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over the Mellor article. The Office Action asserts that, since several piperidine polyhydroxy compounds having various stereochemical configurations are described in the article, piperidine polyhydroxy compounds having the 2S,3R,4R,5S configuration would have been obvious to those skilled in the art. Applicants respectfully traverse the rejection because the unexpected advantages of the compounds defined by the claims were not known in the art at the time the invention was made.

Applicants have surprisingly discovered a class of chemical compounds that are ***specific and selective*** inhibitors of glucosylceramide synthase (GCS). As described in the specification, compounds defined by the claims are selective inhibitors of human GCS, and do not inhibit human β-galactosidase, human β-glucosidase, and human α-glucosidase. See, for example, paragraphs 92 and 93 of the specification as originally filed. In contrast, other known GCS inhibitors, such as N-butyl-deoxynojirimycin (NB-DNJ) and N-butyl-deoxygalactonojirimycin (NB-DGJ), inhibit human β-galactosidase, human β-glucosidase, and human α-glucosidase. For example, as shown in Table 2 of the specification as originally filed, NB-DNJ is a potent inhibitor of human α-glucosidase and also inhibits human β-glucosidase, and NB-DGJ is a potent inhibitor of human β-galactosidase.

Due to their specific and selective inhibition of GCS, compounds defined by the claims can be expected to elicit fewer side effects when administered for the treatment of

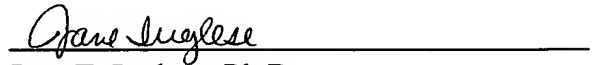
disease states mediated by GCS than would NB-DNJ or NB-DGJ. The selective inhibition of GCS by compounds of formula I, and the expected concomitant reduction in side effects, were not known in the art at the time the invention was made. Accordingly, the subject matter defined by the claims would not have been obvious to those skilled in the art, and Applicants respectfully request withdrawal of the rejection.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, and early and favorable action is respectfully requested.

Respectfully submitted,

Date: November 24, 2004



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